REMARKS

Claims 58-67 are pending. No claims have been added, canceled or amended herein. Accordingly, claims 58-67 will remain pending and under examination upon consideration of this Communication.

In view of the arguments set forth below, applicants maintain that the Examiner's rejections made in the July 12, 2004 Final Office Action have been overcome, and respectfully request that the Examiner reconsider and withdraw same.

The Claimed Invention

The instant invention provides methods and reagents for predicting pregnancy outcome. This invention is based upon the surprising discovery of a correlation between pregnancy outcome and urinary levels of the early pregnancy-associated molecular isoform of hCG. Methods and reagents are provided for the determination of this analyte in a sample.

Double Patenting Rejection

The Examiner rejected claims 58-67 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 53, 59, 60, 65, 71, 72, and 77-82 of U.S. Serial No. 09/017,976, now U.S. Patent No. 6,500,627, for the reasons of record.

In response, applicants will submit a terminal disclaimer at such time as the instant claims are deemed otherwise allowable.

Rejection under 35 U.S.C. §102(e)

The Examiner rejected claims 62 and 67 under 35 U.S.C. §102(e) as allegedly anticipated by Cole et al. (U.S. Patent No. 6,429,018; "Cole").

In response, applicants respectfully traverse for the reasons of record stated in applicants' September 16, 2002 Amendment and April 23, 2004 Communication and for the additional reasons set forth below.

Claim 62 provides a method for determining the amount of an early pregnancy-associated molecular isoform of hyperglycosylated gonadotropin (EPMI-hCG) present in a sample. Claim 67 provides an antibody which binds to EPMI-hCG that is recognized by the B152 antibody.

Under 35 U.S.C. §102, and as stated in M.P.E.P. §2131.01, "[a] claim is anticipated only if *each and every element* as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." (emphasis added). Hence, to anticipate the method of claim 62 and the antibody of claim 67, Cole would have to teach each and every element thereof.

Cole fails to do this.

Cole teaches a prenatal screening method for Down's syndrome by determining the amount of hyperglycosylated gonadotropin (hCG) present in a biological sample from a pregnant woman.

The Examiner asserted that it is proper for the purposes of this rejection to interpret an "early pregnancy associated

molecular isoform of hCG" as a "hyperglycosylated isoform of gonadotropin observed in early pregnancy subjects in Down's syndrome cases", absent a definitive and distinctive characterization of this hCG isoform. To support this assertion, the Examiner relied on the rule that claims are given their broadest possible interpretation consistent with the specification.

In response, applicants assert that the Examiner has given the term "hyperglycosylated isoform of gonadotropin" an interpretation broader than, and inconsistent with the definition taught by Cole itself. Cole specifically limits its definition of hyperglycosylated gonadotropin to "hyperglycosylated gonadotropin, nicked gonadotropin, α-subunits, β-subunits, β-core fragments, and mixtures of any of these which exhibit aberrant carbohydrate profiles and/or aberrant carbohydrate levels as compared to normal levels." (see column 4, lines 37-44). Cole does *not* define a hyperglycosylated gonadotropin to include hCG isoforms present during the *early pregnancy* of a subject. In fact, Cole does not define hCG in relation to *any* specific time period during the pregnancy of the subject.

Furthermore, contrary to the Examiner's position, applicants have provided a definitive and distinctive characterization of the "EPMI-hCG" isoform. The specification, at page 24, lines 2-6, teaches that the present immunoassays were designed "to measure unique early pregnancy-associated molecular isoforms (EPMI) of hCG. These isoforms, likely to differ by carbohydrate composition, are predictive of a successful pregnancy outcome." Thus, the term "EPMI-hCG" has been distinctly characterized within the instant specification. Applicants thus maintain that the hyperglycosylated

gonadotropin taught by Cole does not include the early pregnancy associated isoform of hCG as recited in the instant claims.

Therefore, Cole, at best, teaches a method for determining the amount of hCG present in Down's syndrome cases. Cole fails to teach any method for determining the amount of *EPMI-hCG* present in a sample from a subject. Therefore, Cole fails to teach each and every element of the method of claim 62.

Furthermore, Cole does not teach an antibody which binds to *EPMI-hCG* that is recognized by the B152 antibody deposited with the American Type Culture Collection under Designation No. HB-12467, as taught by claim 67. Cole, at best, teaches that the B152 antibody recognizes nicked hCG obtained from choriocarcinoma patients. Therefore, Cole fails to teach each and every element of the antibody of claim 67.

In view of the above remarks, applicants maintain that claims 62 and 67 satisfy the requirements of 35 U.S.C. §102(e).

Rejections Under 35 U.S.C. §103(a)

The Examiner rejected claims 58-61 under 35 U.S.C. §103(a) as allegedly unpatentable over Cole in view of Birken et al. (Endocrinology, 1993)("Birken").

In response, applicants respectfully traverse.

Claims 58-61 provide a method for predicting pregnancy outcome in a subject.

To establish a *prima facie* case of obviousness, the Examiner must demonstrate three things with respect to each claim. First, the cited references, when combined, must teach or suggest each element of the claim. Second, one of ordinary skill would have been motivated to combine the teachings of the cited references at the time of the invention. And third, there would have been a reasonable expectation that the claimed invention would succeed.

Applicants maintain that the cited references fail to support a *prima facie* case of obviousness because they do not teach or suggest every element of the claimed invention. That is, the cited references fail to teach or suggest methods for predicting pregnancy outcome in a subject by determining the ratio of EPMI-hCG to intact hCG in a sample.

Cole is described above. Birken teaches an analytical method for separating intact hCG from nicked hCG and the hCGβ core fragment using column fractionation. Birken also teaches antibodies B108 and B109 which recognize intact hCG.

The Examiner alleges that it would have been obvious to further incorporate monoclonal antibodies in the immunometric assay method as taught by Cole with the method taught by Birken because Birken specifically taught that use of two-site immunometric assay that separates hCG forms provides advantages in monitoring different complex hCG functions.

Applicants assert that the cited references fail to teach all elements of the claimed method, in that they fail, *inter alia*, to teach methods for predicting pregnancy outcome by determining the ratio of *EPMI-hCG* to intact hCG in a sample. As stated above, Cole fails to teach the detection of *EPMI-hCG*

in a sample. Additionally, Birken also does not teach or suggest *EPMI-hCG*, or a method for its detection. Moreover, neither of the cited references teaches or suggests the element of a *ratio* of EPMI-hCG to intact hCG, as recited in part (c) of claim 58. Thus, the cited references combined fail to teach every element of the rejected claims and therefore the Examiner has failed to establish a *prima facie* case of obviousness.

The Examiner also rejected claims 63-66 under 35 U.S.C. §103(a) as allegedly unpatentable over Cole, in view of Birken, and in further view of Foster et al. (U.S. Patent no. 4,444,879).

In response to the Examiner's rejection, applicants respectfully traverse.

Claims 63-66 provide a diagnostic kit for predicting pregnancy outcome in a subject comprising antibodies which bind to EPMI-hCG.

Cole and Birken are described above. Foster teaches incorporating labels, antibodies, and reagents into a kit format.

Applicants maintain that Foster fails to overcome the deficiencies of Cole and Birken recited above. In particular, Foster does not teach or suggest using EPMI-hCG in a kit format. Thus, the cited references combined fail to teach every element of the rejected claims and therefore the Examiner has failed to establish a *prima facie* case of obviousness.

In view of the above remarks, applicants maintain that claims 58-61 and 63-66 satisfy the requirements of 35 U.S.C. §103(a).

Summary

In view of the remarks made herein, applicants maintain that the claims pending in this application are in condition for allowance. Accordingly, allowance is respectfully requested.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Communication. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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